CLAIMS

What is claimed is:

1. An isolated nucleic acid which encodes a primate MAdCAM.

2. The isolated nucleic acid of Claim 1, wherein the isolated nucleic acid is recombinant.

3. An isolated nucleic acid of Claim 1, wherein said nucleic acid hybridizes under stringent conditions with a second nucleic acid, the second nucleic acid having a nucleotide sequence as shown in Figure 1 (SEQ ID NO:1), Figure 2 (SEQ ID NO:3), or Figure 3 (SEQ ID NO:5).

4. The isolated nucleic acid of Claim 3, wherein said nucleic acid is essentially pure.

5. An isolated nucleic acid of Claim 1, wherein said nucleic acid encodes the polypeptide shown in Figure 1 (SEQ ID NO:2), the polypeptide shown in Figure 2 (SEQ ID NO:4), the polypeptide shown in Figure 3 (SEQ ID NO:6), or the corresponding mature proteins.

6. The isolated nucleic acid of Claim 5, which is a recombinant nucleic acid.

7. The isolated nucleic acid of Claim 5, wherein said nucleic acid is essentially pure.

8. The isolated nucleic acid of Claim 5 having a nucleotide sequence selected from the group consisting of a nucleotide sequence as shown Figure 1 (SEQ ID NO:1), a nucleotide sequence as shown Figure 2 (SEQ ID NO:3), a nucleotide sequence as shown Figure 3 (SEQ ID NO:5), and a portion of any of the foregoing comprising the coding sequence.

9. A recombinant nucleic acid construct comprising a nucleic acid of Claim 1.

10. The recombinant nucleic acid construct of Claim 9, wherein the recombinant nucleic acid is operably linked to an expression control sequence.

11. The recombinant nucleic acid construct of Claim 9 comprising a nucleic acid, wherein said nucleic acid encodes a polypeptide having an amino acid sequence as set forth in Figure 1 (SEQ ID NO:2), Figure 2 (SEQ ID NO:4), Figure 3 (SEQ ID NO:6).

12. The recombinant construct of Claim 11, wherein the nucleic acid is operably linked to an expression control sequence.

13. An isolated primate MAdCAM.

14. The isolated primate MAdCAM of Claim 13, wherein the primate MAdCAM is a human MAdCAM, encoded by a nucleic acid which hybridizes under stringent conditions to a second nucleic acid, the second nucleic acid having a nucleotide sequence as shown in Figure 1 (SEQ ID NO:1) or Figure 2 (SEQ ID NO:3).

15. The isolated primate MAdCAM of Claim 13, wherein the primate MAdCAM is a human MAdCAM as shown in Figure 1 (SEQ ID NO:2), Figure 2 (SEQ ID NO:4), or the corresponding mature protein of either of the foregoing.

16. The isolated primate MAdCAM of Claim 13, wherein the primate MAdCAM is a macaque MAdCAM, encoded by a nucleic acid which hybridizes under stringent conditions to a second nucleic acid, the second nucleic acid having a nucleotide sequence as shown in Figure 3 (SEQ ID NO:5).

17. The isolated primate MAdCAM of Claim 13, wherein the primate MAdCAM is a macque MAdCAM as shown in Figure 3 (SEQ ID NO:6) or the corresponding mature protein.

18. The isolated primate MAdCAM of Claim 15 having essentially an amino acid sequence consisting of amino acids 19-406 of Figure 1 (SEQ ID NO:2), 19-382 of Figure 2 (SEQ ID NO:4) or 22-346 of Figure 3 (SEQ ID NO:6).

19. An isolated primate MAdCAM having one or more functions selected from the group consisting of binding to $\alpha 4\beta 7$ integrin and mediation of cellular adhesion.

20. The isolated primate MAdCAM of Claim 19, wherein cellular adhesion is $\alpha 4\beta 7$ integrin-dependent.

21. The isolated primate MAdCAM of Claim 20, wherein binding is selective for $\alpha 4\beta 7$.

22. A host cell containing a recombinant nucleic acid of Claim 2.

23. The host cell of Claim 22, wherein the nucleic acid is operably linked to an expression control sequence, whereby primate MAdCAM is expressed when the host cell is maintained under conditions suitable for expression.

24. A fusion protein comprising a primate MAdCAM.

25. The fusion protein of Claim 24, comprising a first moiety and a second moiety, wherein said first moiety is a primate MAdCAM and said second moiety is at least a portion of an immunoglobulin chain or variant thereof.

26. The fusion protein of Claim 25, wherein said first moiety is joined at its C-terminal end to the N-terminal end of the second moiety.

27. The fusion protein of Claim 25, wherein the first moiety is selected from the group consisting of a fragment of human MAdCAM containing the entire extracellular domain and a fragment of human MAdCAM containing two N-terminal immunoglobulin domains.

28. The fusion protein of Claim 25, wherein the second moiety is at least a portion of an immunoglobulin heavy chain constant region or variant thereof.

29. The fusion protein of Claim 28, wherein the immunoglobulin heavy chain is of the IgG class.

30. The fusion protein of Claim 28, wherein the second moiety comprises hinge, CH2 and CH3 domains of an immunoglobulin heavy chain.

31. A hybrid immunoglobulin comprising a fusion protein of Claim 25.

32. A hybrid immunoglobulin comprising a fusion protein of Claim 31, wherein said hybrid immunoglobulin is a homodimer.

33. A nucleic acid construct comprising a nucleic acid containing a coding sequence which encodes a fusion protein of Claim 24, wherein optionally the coding sequence is operably linked to an expression control sequence.

34. A nucleic acid construct, comprising a nucleic acid containing a sequence which encodes a fusion protein of Claim 25, wherein optionally the coding sequence is operably linked to an expression control sequence.

35. A method for producing a primate MAdCAM comprising:

(a) introducing into a host cell a nucleic acid construct comprising a nucleic acid which encodes a primate MAdCAM, whereby a recombinant host cell is produced having said coding sequence operably linked to at least one expression control sequence; and

(b) maintaining the host cells produced in step (a) in a suitable medium under conditions whereby the nucleic acid is expressed.

36. The method of Claim 35, further comprising the step of isolating primate MAdCAM.

37. A method for producing a primate MAdCAM comprising maintaining a host cell containing a recombinant nucleic acid encoding a primate MAdCAM under conditions suitable for expression of the nucleic acid, whereby primate MAdCAM is produced.

38. The method of Claim 37 further comprising the step of isolating primate MAdCAM.

39. An antibody or functional portion thereof which binds primate MAdCAM.

40. The antibody of Claim 39, wherein said antibody can inhibit one or more functions of a primate MAdCAM.

41. The antibody of Claim 39, wherein said antibody can selectively inhibit $\alpha 4\beta 7$-dependent adhesion.

42. The antibody of Claim 40, wherein the primate is a human.

43. A method of detecting a selected primate MadCAM in a sample comprising:

a) contacting a sample with an antibody which binds an isolated primate MAdCAM under conditions suitable for specific binding of said antibody to the selected primate MAdCAM; and

c) detecting antibody-MAdCAM complexes.

44. A method of detecting or identifying a ligand of or an agent which binds a primate MAdCAM comprising combining an agent to be tested with an isolated primate MAdCAM under conditions suitable for binding of ligand thereto, and detecting or measuring the

formation of a complex between said agent and primate MAdCAM.

45. A method of detecting or identifying a ligand of or an agent which binds a primate MAdCAM comprising:

a) combining an agent to be tested with a host cell expressing recombinant primate MAdCAM under conditions suitable for binding of ligand thereto; and

b) detecting or measuring the formation of a complex between said agent and the primate MAdCAM.

46. A method of detecting an inhibitor of binding of primate MAdCAM to a ligand thereof comprising:

a) combining an agent to be tested with a ligand of primate MAdCAM and a composition comprising isolated and/or recombinant primate MAdCAM under conditions suitable for binding of ligand thereto; and

b) detecting or measuring binding between primate MAdCAM and ligand, whereby decreased binding as compared with a suitable control indicates that the agent is an inhibitor.

47. The method of Claim 46, wherein the isolated and/or recombinant primate MAdCAM is a fusion protein.

48. The method of Claim 46, wherein the composition comprising isolated and/or recombinant primate MAdCAM contains a host cell expressing recombinant primate MAdCAM.

49. A method of detecting an inhibitor of cellular adhesion mediated by MAdCAM, comprising:
a) combining an agent to be tested, a first cell expressing a recombinant primate MAdCAM, and a second cell bearing an $\alpha 4\beta 7$ integrin under conditions suitable for adhesion of said first cell to said second cell; and
b) detecting or measuring adhesion between said first and second cells, whereby decreased adhesion as compared with a suitable control indicates that the agent is an inhibitor.

50. The method of Claim 49 wherein the agent an antibody or antibody fragment.

51. A method of treating an individual having a disease associated with leukocyte infiltration of tissues expressing the molecule MAdCAM, comprising administering to the individual an effective amount of an antibody which can inhibit the binding of leukocytes to MAdCAM.

52. The method of Claim 51 wherein the disease is a disease associated with leukocyte recruitment to the gastrointestinal tract or other tissues as a result of binding of leukocytes to gut-associated endothelium expressing the molecule MAdCAM, and the antibody can inhibit the binding of leukocytes to endothelial MAdCAM.

53. The method of Claim 52 wherein antibody is a monoclonal antibody or an antigen binding fragment thereof.

54. The method of Claim 53 wherein the monoclonal antibody or antigen binding fragment thereof inhibits adhesion of leukocytes expressing an integrin containing the $\beta 7$ chain and endothelium expressing MAdCAM.

55. The method of Claim 54 wherein the monoclonal antibody or antigen binding fragment thereof binds $\alpha 4\beta 7$ integrin.

56. The method of Claim 55 wherein the monoclonal antibody or antigen binding fragment thereof binds $\beta 7$.

57. The method of Claim 56 wherein the monoclonal antibody or antigen binding fragment thereof binds MAdCAM.

58. The method of Claim 54 wherein the monoclonal antibody or antigen binding fragment thereof has the antigenic specificity of a monoclonal antibody selected from the group consisting of FIB 21, FIB 30, FIB 504 and ACT-1.

59. The method of Claim 58 wherein the monoclonal antibody or antigen binding fragment thereof is selected from the group consisting of FIB 21, FIB 30, FIB 504 and ACT-1 or antigen binding fragments thereof.

60. The method of Claim 59 wherein the monoclonal antibody is ACT-1.

61. The method of Claim 54 wherein the monoclonal antibody is selected from the group consisting of a chimeric antibody and a humanized antibody.

62. The method of Claim 54 wherein the leukocytes are lymphocytes.

63. The method of Claim 54 wherein the leukocytes are monocytes.

64. The method of Claim 54 wherein the disease is inflammatory bowel disease.

65. The method of Claim 64 wherein the disease is ulcerative colitis.

66. The method of Claim 64 wherein the disease is Crohn's disease.

67. The method of Claim 64 wherein the disease is Celiac disease, enteropathy associated with seronegative arthropathies, microscopic or collagenous colitis, eosinophilic gastroenteritis, or pouchitis.

68. The method of Claim 64 wherein the monoclonal antibody or antigen binding fragment thereof binds $\alpha 4\beta 7$.

69. The method of Claim 64 wherein the monoclonal antibody or antigen binding fragment thereof binds MAdCAM.

70. The method of Claim 64 wherein the monoclonal antibody or antigen binding fragment thereof has the antigenic specificity of a monoclonal antibody selected from the group consisting of FIB 21, FIB30, FIB 504 and ACT-1.

71. The method of Claim 70 wherein the monoclonal antibody or antigen binding fragment thereof is selected from the group consisting of FIB 21, FIB30, FIB 504 and ACT-1 or antigen binding fragments thereof.

72. The method of Claim 71 wherein the monoclonal antibody is ACT-1.

73. The method of Claim 64 wherein the monoclonal antibody is selected from the group consisting of a chimeric antibody and a humanized antibody.

74. The method of Claim 64 wherein more than one monoclonal antibody which inhibits the binding of leukocytes to endothelial MAdCAM is administered.

75. The method of Claim 64 wherein more than one monoclonal antibody which inhibits the binding of leukocytes to endothelial ligands is administered.

76. The method of Claim 75 wherein at least one monoclonal antibody inhibits the binding of leukocytes to an endothelial ligand other than MAdCAM.

77. A method for treating inflammatory bowel disease in an individual comprising administering to the individual an effective amount of an antibody which binds endothelial MAdCAM or the $\alpha 4\beta 7$ integrin.

78. The method of Claim 77 wherein antibody is a monoclonal antibody or an antigen binding fragment thereof.

79. The method of Claim 78 wherein the monoclonal antibody or antigen binding fragment thereof binds $\alpha 4\beta 7$ integrin.

80. The method of Claim 79 wherein the monoclonal antibody or antigen binding fragment thereof binds $\beta 7$.

81. The method of Claim 78 wherein the monoclonal antibody or antigen binding fragment thereof binds MAdCAM.

82. The method of Claim 78 wherein the monoclonal antibody or antigen binding fragment thereof has the antigenic specificity of a monoclonal antibody selected from the group consisting of FIB 21, FIB 30, FIB 504 and ACT-1.

83. The method of Claim 82 wherein the monoclonal antibody or antigen binding fragment thereof is selected from the group consisting of FIB 21, FIB 30, FIB 504 and ACT-1 or antigen binding fragments thereof.

84. The method of Claim 83 wherein the monoclonal antibody is ACT-1.

85. The method of Claim 78 wherein the monoclonal antibody is selected from the group consisting of a chimeric antibody and a humanized antibody.

86. The method of Claim 78 wherein the disease is ulcerative colitis.

87. The method of Claim 78 wherein the disease is Crohn's disease.

88. The method of Claim 78 wherein the disease is Celiac disease, enteropathy associated with seronegative arthropathies, microscopic or collagenous colitis, eosinophilic gastroenteritis, or pouchitis.

89. A method of treating a primate having a disease associated with leukocyte infiltration of tissues expressing the molecule MAdCAM-1, comprising administering an effective amount of an antibody having specificity for a primate MAdCAM.

90. The method of Claim 89, wherein the antibody can inhibit the interaction a primate MAdCAM with an $\alpha 4\beta 7$ integrin.

91. The method of Claim 89, wherein the disease is a disease associated with leukocyte infiltration of tissues as a result of binding of leukocytes to gut-associated endothelium expressing the molecule MAdCAM.

92. A method for treating inflammatory bowel disease in a primate, comprising administering to the primate an effective amount of an antibody which binds a primate MAdCAM.

93. The method of Claim 92, wherein the antibody can inhibit the interaction a primate MAdCAM with an $\alpha 4\beta 7$ integrin.

94. A method of treating a primate having a disease associated with leukocyte infiltration of tissues expressing the molecule MAdCAM-1, comprising administering an effective amount of a primate MAdCAM or a hybrid immunoglobulin comprising a primate MAdCAM.

95. The method of Claim 94, wherein the primate MAdCAM or a hybrid immunoglobulin comprising a primate MAdCAM can inhibit the interaction a primate MAdCAM with an $\alpha 4\beta 7$ integrin.

96. The method of Claim 94, wherein said hybrid immunoglobulin contains a fusion protein, comprising a first moiety and a second moiety, wherein said first moiety is a primate MAdCAM and said second moiety is at least a portion of an immunoglobulin chain.

97. The method of Claim 94, wherein the disease is a disease associated with leukocyte infiltration of tissues as a result of binding of leukocytes to gut-associated endothelium expressing the molecule MAdCAM.

98. A method for treating inflammatory bowel disease in a primate, comprising administering to the primate an effective amount of a primate MAdCAM or a hybrid immunoglobulin comprising a primate MAdCAM.

99. The method of Claim 98, wherein the primate MAdCAM or a hybrid immunoglobulin comprising a primate MAdCAM can inhibit the interaction a primate MAdCAM with an $\alpha 4\beta 7$ integrin.

100. The method of Claim 98, wherein said hybrid immunoglobulin contains a fusion protein, comprising a first moiety and a second moiety, wherein said first moiety is a primate MAdCAM and said second moiety is at least a portion of an immunoglobulin chain.